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ORIGINAL ARTICLE

Predictors of Donor Follow-Up After Living Donor Liver Transplantation

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Donor safety in living liver donation is of paramount importance; however, information on long-term outcomes is limited by incomplete follow-up. We sought to ascertain factors that predicted postdonation follow-up in 456 living liver donors in the Adult-to-Adult Living Donor Liver Transplantation Cohort Study. Completed donor follow-up was defined as physical, phone, or laboratory contact at a given time point. Univariate and multivariate mixed effects logistic regression models, using donor and recipient demographic and clinical data and donor quality-of-life data, were developed to predict completed follow-up. Ninety percent of the donors completed their follow-up in the first 3 months, and 83% completed their follow-up at year 1; rates of completed follow-up ranged from 57% to 72% in years 2 to 7 and from 41% to 56% in years 8 to 10. The probability of completed follow-up in the first year was higher for white donors [odds ratio (OR) = 3.27, 95% confidence interval (CI) = 1.25-8.58] but lower for donors whose recipients had hepatitis C virus or hepatocellular carcinoma (OR = 0.34, 95% CI = 0.17-0.69). After the first year, an older age at donation predicted more complete follow-up. There were significant center differences at all time points (OR range = 0.29-10.11), with center variability in both returns for in-center visits and the use of phone/long-distance visits. Donor follow-up in the first year after donation was excellent but decreased with time. Predictors of follow-up varied with the time since donation. In conclusion, adapting best center practices (enhanced through the

Abbreviations: A2ALL, Adult-to-Adult Living Donor Liver Transplantation Cohort Study; CI, confidence interval; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HRQOL, health-related quality of life; LDLT, living donor liver transplantation; MCS, Mental Component Score; OPTN, Organ Procurement and Transplantation Network; OR, odds ratio; PCS, Physical Component Score; QOL, quality of life; SD, standard deviation; SF-36, Short Form 36; SRTR, Scientific Registry of Transplant Recipients; UNOS, United Network for Organ Sharing.

This study was presented in part at the 12th annual meeting of the American Transplant Congress (Boston, MA, June 2-6, 2011).

The data reported here were supplied by the Minneapolis Medical Research Foundation as the contractor for the Scientific Registry of Transplant Recipients. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the Scientific Registry of Transplant Recipients or the US Government.

This is publication number 24 of the Adult-to-Adult Living Donor Liver Transplantation Cohort Study. The Adult-to-Adult Living Donor Liver Transplantation Cohort Study Group includes the following: Northwestern University (Chicago, IL); University of California Los Angeles (Los Angeles, CA); University of California San Francisco (San Francisco, CA); University of Colorado Health Sciences Center (Denver, CO); University of North Carolina (Chapel Hill, NC); Epidemiology and Clinical Trials Branch, Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health (Bethesda, MD); University of Michigan (Ann Arbor, MI); Department of Surgery, Columbia Presbyterian Medical Center (New York, NY); University of Pennsylvania (Philadelphia, PA); Department of Internal Medicine, University of Virginia (Charlottesville, VA); and Virginia Commonwealth University (Richmond, VA).

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use of telephones and social media) to maintain contact with donors represents a significant opportunity to gain valuable information about long-term donor outcomes. *Liver Transpl 20:967-976, 2014*. © **2014 AASLD.**

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Donor safety is of paramount importance in assessing the success of living donor liver transplantation (LDLT). To date, most data have focused on short-term outcomes, including death and surgical complications such as bile leakage.[1-4] A wide range of complication rates have been reported for donors after LDLT. Overall, reported complication rates have ranged from 0% to 67%, with an overall crude complication rate in a meta-analysis and the large National Institutes of Health–funded Adult-to-Adult Living Donor Liver Transplantation Cohort Study (A2ALL) experience of approximately 38%.[5-7] Studies assessing donor health-related quality of life (HRQOL) after LDLT have also yielded variable findings, although most have demonstrated that HRQOL (assessed with generic instruments not specific to LDLT) is at or above US norms.[8] These studies also have consistently found that nearly all donors state that they would donate again, regardless of recipient outcomes.[8-12] Nevertheless, 71% of donors have reported abdominal symptoms several months after the operation that they attributed to the donation surgery,[10] and it is clear that psychological distress is relatively common in both liver and kidney donors.[13]

Longer term follow-up is particularly important and may identify areas that may be sources of stress and concern to donors, including finances[14] and the incidence of long-term psychiatric disturbances.[15] To accurately determine the effects of donation on living liver donors, it is important for transplant centers to maintain contact with donors over the long-term. Currently, 2 years' follow-up is mandated for the United Network for Organ Sharing (UNOS) reporting requirements, but this may inadequately capture the impact on long-term donor HRQOL and health. In order to acquire these data and ensure continued donor follow-up and complete data, state-of-the art methods need to be implemented. These methods have not been implemented in most prior studies. One of the barriers to obtaining high-quality long-term data from donors is the variable practice patterns of centers following donors after living donation with respect to the frequency and duration of visits after LDLT.[16] In addition, years after LDLT, donors may be lost to follow-up or difficult to contact because of a real or perceived lack of need for medical care, insurance and financial barriers, or a lack of access to care. The issues that determine whether donors will or will not pursue long-term follow-up are likely multifactorial and include donor, recipient, and center factors, but these issues have not been systematically studied.

Using the multicenter A2ALL cohort study, we investigated the factors associated with donor contact with transplant centers for the purpose of A2ALL study follow-up. The objective of this study was to assess the characteristics that make donors more likely to maintain contact with their transplant centers with the goal of improving donor follow-up in future clinical care as well as research settings. This is particularly timely because UNOS is considering mandating new thresholds for complete follow-up for living donors in the future.

PATIENTS AND METHODS

Data Collection

The A2ALL study collected prospective data on living liver donors and their recipients enrolled at 9 US transplant centers between 2004 and 2009. Prospective living liver donors as well as previous living liver donors who donated after January 1, 1998 were eligible for enrollment. According to the clinical A2ALL protocol, donors were scheduled to return to the transplant center for postdonation follow-up at 1 week, 1 month, 3 months, 12 months, and annually thereafter. For donors who enrolled after donation, protocol study visits began at the corresponding postdonation time point; thus, the expected number of visits per donor varied according to when they were enrolled. The duration of A2ALL follow-up was beyond the standard clinical follow-up protocol for donors at most centers. When donors were unable to return to the transplant center for a study visit, coordinators attempted to contact subjects via phone and mail, and donors were asked to send local laboratory results to the transplant center. These methods of remote follow-up were similar to methods of follow-up allowable for the Organ Procurement and Transplantation Network (OPTN) data collection.

For this analysis, completed follow-up was defined as the collection of any data on the donor's status by any method since the last prospective assessment. The information could be obtained during a clinical visit or by telephone, e-mail, post mail, or other means when a visit was not possible. Further categorization was performed according to whether data were collected during an actual clinic visit or with other methods only. The expected follow-up visit dates were calculated from the transplant date, and visit window endpoints were halfway between adjacent expected visit dates. Expected visits were included in the analysis only if the donor had consented to the study before the start of the window and had not withdrawn consent or died before the end of the window. This rule was followed regardless of whether or not a visit occurred because it was too difficult to determine whether a visit should have been expected if the subject had not been enrolled for the entire window. For example, there were 4 protocol visits in the

first year (at 1 week, 1 month, 3 months, and 1 year); however, a donor who enrolled in the month 1 window would have only 2 expected visits in the first year because of the timing of the enrollment.

For each donor, recipient information, including diagnoses and dates of retransplantation and death, was obtained from the A2ALL recipient database. When such information was not available, this study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States; these data are submitted by the members of OPTN and have been described elsewhere. The Health Resources and Services Administration (US Department of Health and Human Services) provides oversight for the activities of the OPTN and SRTR contractors.

HRQOL surveys, including the Short Form 36 (SF-36; version 2), were administered to donors before donation. The SF-36 was additionally administered 3 and 12 months after donation and annually thereafter. Donors who had enrolled after donation were administered the SF-36 at the first postdonation study visit after their enrollment. The HRQOL surveys were administered in several formats (on tablet computers, via paper forms either by mail or at the clinical center, by telephone, or with a Web-based format) to maximize responses. The Mental Component Score (MCS) and the Physical Component Score (PCS), calculated from the SF-36 survey, were standardized to the US population distribution [average = 50, standard deviation (SD) = 10].

The study was approved by the institutional review boards and privacy boards of the University of Michigan Data Coordinating Center and each of the 9 participating transplant centers. All subjects provided written informed consent for this study.

Statistical Analysis

Descriptive statistics included means, SDs, and proportions. The means, SDs, and interquartile ranges of the numbers of expected and completed follow-up visits were calculated for the visits from the first week through the first year, for every subsequent 3-year period, and overall. The proportion of donors who completed follow-up at each postdonation study time point was graphed with standard error bars based on the binomial distribution along with center-specific proportions at each time point for which a given center had at least 5 expected visits. The proportion of donors who completed any type of follow-up (including in-person, phone, and e-mail contact) and the proportion who completed follow-up clinic visits at the transplant center were also graphed by transplant center. Finally, centers were divided into 2 groups: those that had at least 80% follow-up and those with <80% follow-up. The percentages of follow-up completed at the clinic and by other means were graphed by time point for these 2 groups.

The probability of completed follow-up was modeled with multivariate repeated measures logistic regression to account for multiple measurements of the same subject over time. Completed follow-up through the first year (month 1, month 3, and year 1) was modeled separately from completed follow-up at year 2 and subsequent annual follow-up (through year 10) because different covariates were important in the earlier time periods versus the later time periods. Week 1 was not included in the models because every subject had completed follow-up at this time. The 2 highest performing centers were combined because of small cell counts. These centers were both in large cities with ethnically diverse populations. The within-subject correlation across study visits was modeled with a 4-parameter Toeplitz covariance structure.[16] Variables considered for inclusion included the following: donor demographics (sex, ethnicity, race, age at donation, and education level), relationship with the recipient (spouse, immediate family, or other), surrogate for the distance from the transplant center (living in the same state or a state contiguous to the state of the transplant center versus living in a more distant state; only the donor's state of residence—not the distance from the transplant center—was collected), indicator variable for each transplant center, transplant center volume (3-year average for the visit year and the 2 prior years), complications in the first year after donation (Clavien grade 2 or higher or Clavien grade 3 or higher), recipient diagnosis [hepatitis C virus (HCV) or hepatocellular carcinoma (HCC), alcohol-related diagnosis, cholestatic cirrhosis, or other], recipient outcomes (graft loss or death in the prior year or in any previous year), and number of years from donation. To estimate the amount of variation in follow-up explained by center effects, we separately modeled the month 3, year 1, and year 2 time points with logistic regression and compared the generalized R^2 statistic between models with and without center effects.

Seven of the 9 participating centers (those whose participation continued in the second phase of A2ALL) submitted information on their standard-of-care follow-up schedule for living liver donors. Indicators for whether follow-up was required at the transplant center beyond 1 month and 2 years after donation were also tested in the models. For the subset of donors for whom HRQOL data were available, the PCS and the MCS from the SF-36 were tested as potential time-dependent predictors of completed follow-up in a separate logistic regression model. Models were fit with PCS and MCS values from the previous visit to predict completed follow-up at the next visit. In these models, because of the smaller number of donors with HRQOL data and the limited number of usable visits per donor, the within-subject correlation was modeled with the single-parameter compound symmetry covariance structure.[16] Variables with P values less than 0.1 were considered significant for all previously described models from above. All analyses were conducted with SAS 9.2 software (SAS Institute, Inc., Cary, NC).

TABLE 1. Characteristics of Donors Who Donated at Centers With <80% or ≥80% Follow-Up

	Overall (n = 456)		<80% Follow-Up (n = 280)		≥80% Follow-Up (n = 176)		
	n or Mean	% or SD (Range)	n or Mean	% or SD (Range)	n or Mean	% or SD (Range)	*P* Value*
Age at donation (years)	38.0	10.3 (18-63)	39.2	10.4 (18-63)	36.0	9.9 (19-55)	0.001
Sex							0.90
Male	216	47%	132	47%	84	48%	
Female	240	53%	148	53%	92	52%	
Race							0.07
Nonwhite	54	12%	27	10%	27	15%	
White	402	88%	253	90%	149	85%	
Ethnicity							0.05
Non-Hispanic/non-Latino	389	85%	246	88%	143	81%	
Hispanic/Latino	67	15%	34	12%	33	19%	
Total education							0.68
Grade school or high school	96	21%	59	21%	37	21%	
Attended college/technical school	122	27%	78	28%	44	25%	
Associate, bachelor, or postcollege graduate degree	183	40%	122	44%	61	35%	
Unknown	55	12%	21	8%	34	19%	
Relationship with recipient							0.09
Spouse	53	12%	39	14%	14	8%	
Immediate family (parent, child, or full sibling)	251	55%	145	52%	106	60%	
Other	152	33%	96	34%	56	32%	
Distance from center							0.87
Within 1 US state of transplant center	367	80%	226	81%	141	80%	
>1 US state from transplant center	89	20%	54	19%	35	20%	
Complication in first year	124	27%	83	30%	41	23%	0.14
Grade 2 or higher complication in first year	86	19%	61	22%	25	14%	0.04
Grade 3 or higher complication in first year	2	0%	2	1%	0	0%	0.53
Recipient death	77	17%	50	18%	27	15%	0.49
Recipient graft failure	114	25%	73	26%	41	23%	0.51
Recipient diagnosis†							
HCV/HCC	204	45%	115	41%	89	51%	0.05
Alcohol-related liver disease	52	11%	34	12%	18	10%	0.53
Cholestatic cirrhosis	130	29%	84	30%	46	26%	0.37
Other diagnosis	222	49%	144	51%	78	44%	0.14

*The *t* test was used for continuous variables, and the chi-square test or Fisher's exact test was used for categorical variables. The tests were used to compare subjects at centers with <80% follow-up and subjects at centers with ≥80% follow-up.

†Recipients could have more than 1 diagnosis, so the percentages may not add up to 100.

RESULTS

There were 456 donors included in the analysis, with scheduled postdonation study visits ranging from 1 week to 10 years after donation. At donation, the mean age was 38 years (range = 18-63 years). The majority was female and white, had education beyond high school, and donated to a spouse or immediate family member (Table 1). The leading diagnoses of the recipients of the living donor grafts included HCV or HCC (45%) and cholestatic cirrhosis (29%). Graft failure (defined as retransplantation or death) was observed in 25% of the recipients during follow-up. Complications occurred in 27% of the donors in the first year after donation, and 19% had Clavien grade 2 or higher complications during this time period.

Three centers comprising 176 donors had at least 80% follow-up (high–follow-up centers), and the remaining 6 centers comprising 280 donors had less than 80% follow-up (low–follow-up centers) (Tables 1 and 2). We chose 80% as the cutoff because it is suggested in the OPTN guidance document for living donor follow-up.[17] Donors at high–follow-up centers were significantly younger than those at low–follow-up centers (mean age: 36.0 versus 39.2 years, $P = 0.001$), and they had fewer grade 2 or higher complications in the first year (14% versus 22%, $P = 0.04$).

TABLE 2. QOL Data for Donors Who Donated at Centers With <80% or ≥80% Follow-Up

	Overall (n = 456)		<80% Follow-Up (n = 280)		≥80% Follow-Up (n = 176)		
	n or Mean	% or SD (Range)	n or Mean	% or SD (Range)	n or Mean	% or SD (Range)	*P* Value*
Subjects with eligible SF-36 forms†	265	58%	151	54%	114	65%	0.02
Average number of SF-36 forms per donor	1.8	1.0 (1-4)	1.5	0.8 (1-4)	2.2	1.1 (1-4)	<0.001
Average PCS‡	54.1	7.7 (21-70)	54.1	6.8 (23-63)	54.2	8.4 (21-70)	0.92
Average MCS‡	52.0	9.5 (−1 to 68)	52.6	8.9 (12-64)	51.4	10.0 (−1 to 68)	0.15

*The *t* test was used for continuous variables, and the chi-square test or Fisher's exact test was used for categorical variables. The tests were used to compare subjects at centers with <80% follow-up and subjects at centers with ≥80% follow-up.
†Eligible SF-36 forms included forms completed at postdonation visits when the subject had at least 1 more expected postdonation visit after the visit during which the SF-36 form was completed.
‡The scores have been normalized to the US population mean and SD (50 and 10, respectively).

TABLE 3. Distribution of Expected Visits and Completed Follow-Up

	Mean per Subject	SD	25th Percentile	75th Percentile
Overall (n = 456 donors)				
Expected visits	4.45	1.43	3.00	5.00
Completed follow-up visits	3.52	1.63	3.00	5.00
Mean of expected donor follow-up completed	79%	26%	60%	100%
Through year 1 (n = 283 donors)*				
Expected visits	3.56	0.79	3.00	4.00
Completed follow-up visits	3.35	0.88	3.00	4.00
Mean of expected donor follow-up completed	94%	14%	100%	100%
Years 2-4 (n = 239 donors)*				
Expected visits	1.97	0.83	1.00	3.00
Completed follow-up visits	1.31	0.94	1.00	2.00
Mean of expected donor follow-up completed	66%	40%	33%	100%
Years 5-7 (n = 180 donors)*				
Expected visits	2.16	0.82	1.00	3.00
Completed follow-up visits	1.42	1.02	1.00	2.00
Mean of expected donor follow-up completed	64%	39%	33%	100%
Years 8-10 (n = 89 donors)*				
Expected visits	1.80	0.81	1.00	2.00
Completed follow-up visits	0.96	0.95	0.00	2.00
Mean of expected donor follow-up completed	51%	45%	0%	100%

NOTE: Donors could consent at any time after donation, so the number of expected visits within a year for a given donor did not necessarily equal the total number of possible expected protocol study visits within that same year.
*Number of donors who had at least 1 expected visit within the given time range.

As stated previously, donors were expected to attend in-person clinic visits at postdonation times specified by the protocol; any follow-up with the donor, including phone contact, was considered completed follow-up in this analysis. Donors could enroll at any time before or after donation, so the number of expected visits varied by donor because of the differing entry and exit points in the study. Donors had an average of 3.52 completed visits and 4.45 expected visits (mean = 79%) during the time that they were enrolled in the study (interquartile range for both completed and expected visits = 3-5; Table 3). Donors with expected visits in the first year after donation (n = 283) had on average 3.35 completed visits and 3.56 expected visits (mean = 94%, interquartile range for both = 3-4). In postdonation years 2 to 4, 5 to 7, and 8 to 10, the average numbers of completed visits and expected visits per donor were 1.31 and 1.97 (mean = 66%), 1.42 and 2.16 (mean = 64%), and 0.96 and 1.80 (mean = 51%), respectively.

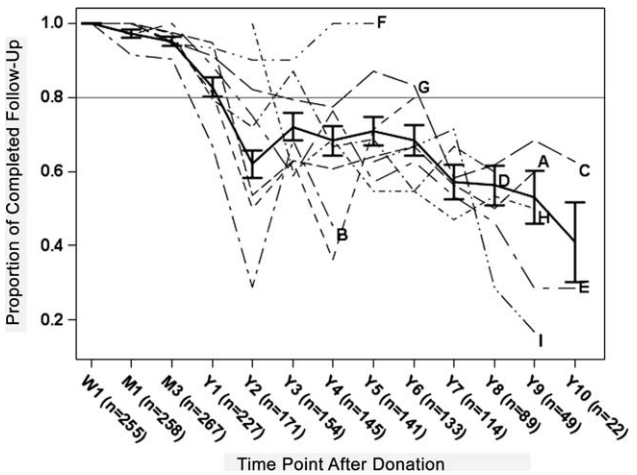

Figure 1. Overall proportion of donors with completed follow-up among those with expected follow-up by time point (solid line) with ±1 standard error bars. The proportions of donors with completed follow-up by center (dashed or dotted lines) are also shown for the 9 A2ALL centers (labeled A-I) at time points with at least 5 expected visits. The time points after donation were week 1 (W1), month 1 (M1), month 3 (M3), and years 1 to 10 (Y1-Y10).

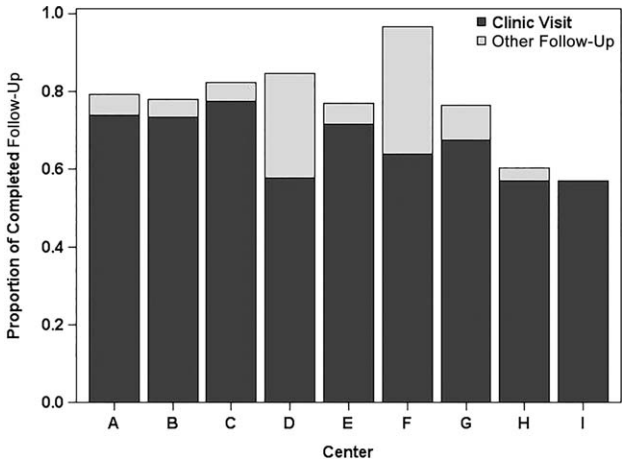

Figure 2. Proportions of expected follow-up achieved via clinic visits and other follow-up methods by center for all time points combined. Other follow-up included contact with donors via phone, e-mail, post mail, or local laboratory testing. Centers are ordered by the total living donor volume (descending) for 1998-2010.

Completed follow-up occurred for more than 90% of the protocol study visits in the first several months after donation, and then this dropped to 83% at 1 year and 62% at 2 years after donation (Fig. 1). The percentage of completed follow-up remained steady between 57% and 72% until 7 years after donation and then decreased steadily until 10 years after donation. Although there was some variability among the 9 centers, the trends were similar over time.

The overall percentage of completed follow-up (clinic visits and other follow-up) varied greatly by center and ranged from 57% to 97% (Fig. 2). The percentage of completed clinic visits was less varied and ranged

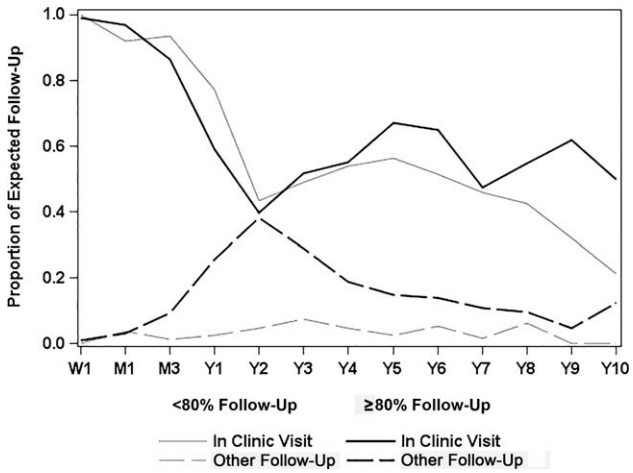

Figure 3. Percentages of in-person follow-up (top lines) and other follow-up (eg, phone or e-mail; bottom lines) by groups of centers that averaged <80% of expected follow-up (gray lines) and centers that averaged ≥80% of expected follow-up (black lines). The time points after donation were week 1 (W1), month 1 (M1), month 3 (M3), and years 1 to 10 (Y1-Y10).

from 57% to 77%. Centers with high and low follow-up had similar proportions of completed in-clinic visits up to year 2, after which high–follow-up centers had slightly higher rates of in-clinic follow-up (Fig. 3). The proportion of other follow-up rose between month 1 and year 2 for high–follow-up centers, and this compensated for the decrease in in-clinic follow-up, whereas for low–follow-up centers, the proportion of other follow-up remained at approximately 5% for the duration of the study. Differences in the use of long-distance visits made the biggest contribution to center variability in achieving donor follow-up. The high–follow-up centers were able to increase their proportion of follow-up achieved by 10% to 30% through the use of other methods of follow-up.

Predictors of completed follow-up in the first year (corresponding to study time points at month 1, month 3, and year 1 after donation) included the following: race, diagnosis of HCV or HCC, indicators for months since donation, and transplant center (Table 4). Donors of white race were more likely to complete their follow-up during this early time period [odds ratio (OR) = 3.27, 95% confidence interval (CI) = 1.25-8.58], whereas donors whose recipients had diagnoses of either HCV or HCC were less likely to complete follow-up (OR = 0.34, 95% CI = 0.17-0.69). Donors were more likely to complete their follow-up in the first and third months after donation in comparison with the first year after donation, and the follow-up during this early time period varied by center (Table 4). Centers with higher living donor volumes (in the absence of transplant center indicators) had a significantly lower probability of completed follow-up (OR per 10-case higher volume = 0.31, 95% CI = 0.15-0.66). For the centers for which the information was available, there was no statistical evidence that a clinical standard of requiring follow-up beyond 1 month resulted in donors being more likely to return for follow-up. These estimates

TABLE 4. Probability of Completed Follow-Up in the First Year Modeled With Repeated Measures Logistic Regression

Predictor	OR	Lower 95% Confidence Limit	Upper 95% Confidence Limit	*P* Value
White race*	3.27	1.25	8.58	0.02
Recipient diagnosis of HCV or HCC†	0.34	0.17	0.69	0.003
Time after donation‡				
Month 1	9.23	4.21	20.24	<0.001
Month 3	4.84	2.55	9.16	<0.001
Center§				
A/H	3.31	1.05	10.45	0.04
B	0.21	0.11	0.40	<0.001
C	1.26	0.54	2.95	0.59
D	0.88	0.35	2.24	0.79
E	1.73	0.57	5.29	0.33
F	1.36	0.23	8.13	0.73
G	0.55	0.20	1.54	0.25

*The reference is nonwhite race.
†The reference is all other diagnoses.
‡The reference is year 1.
§One center was excluded from this model because it did not have any new donors during the prospective era. The reference was the overall mean.

TABLE 5. Probability of Completed Follow-Up in Years 2 to 10 Modeled With Repeated Measures Logistic Regression

Predictor	OR	Lower 95% Confidence Limit	Upper 95% Confidence Limit	*P* Value
Donor age at donation per 10 years	1.20	1.02	1.41	0.03
Year after donation*				
3	1.42	0.88	2.30	0.15
4	1.13	0.68	1.88	0.63
5	1.11	0.65	1.90	0.69
6	0.93	0.55	1.57	0.79
7	0.47	0.28	0.80	0.005
8	0.48	0.27	0.86	0.01
9	0.39	0.20	0.77	0.006
10	0.24	0.10	0.59	0.002
Center†				
A	0.69	0.45	1.05	0.08
B	0.29	0.17	0.47	<0.001
C	1.76	1.19	2.60	0.005
D	1.13	0.71	1.78	0.61
E	0.80	0.50	1.30	0.37
F	10.11	3.19	32.00	<0.001
G	0.49	0.27	0.89	0.02
H	0.77	0.55	1.08	0.13
I	0.84	0.60	1.17	0.31

*The reference is year 2.
†The reference is the overall mean.

remained largely unchanged when prior recipient death and retransplantation were added to the model. Although not significant, prior recipient death and retransplantation were associated with a higher probability of completed follow-up (OR for death = 1.33, 95% CI = 0.44-3.97; OR for retransplantation = 2.29, 95% CI = 0.46-11.46). The results were similar when recipient graft failure (defined as the first of death or retransplantation) was included in the model (OR = 1.74, 95% CI = 0.64-4.70).

Predictors of completed follow-up beyond the first year included the following: age at donation,

indicators for the number of years after donation, and transplant center (Table 5). Older donors were more likely to complete follow-up (OR per 10 years = 1.20, 95% CI = 1.02-1.41). The probabilities of completed follow-up in the third, fourth, and fifth years after donation were similar to the probability in the second year, but from the sixth year on, follow-up became less and less likely. Again, completed follow-up varied greatly by transplant center (OR range = 0.29-10.11 versus the overall mean). In contrast to follow-up in the first year, however, the center living donor volume was not significantly associated with completed follow-up when it was tested in the absence of center indicators (OR per 10-case higher volume = 0.86, 95% CI = 0.64-1.17). An indicator for whether the center's clinical standard required follow-up beyond 2 years was also tested, and again, no relationship was shown between this clinical standard and higher rates of follow-up. Similarly to the early postdonation analysis, the addition of prior recipient death and retransplantation did not substantively change the estimates. Recipient death was associated with no change in the probability of completed follow-up (OR = 1.00, 95% CI = 0.60-1.66), and recipient retransplantation was associated with a nonsignificantly higher probability of completed follow-up (OR = 1.44, 95% CI = 0.84-2.49). The results were also similar for recipient graft failure (OR = 1.10, 95% CI = 0.73-1.67).

Because center effects were highly significant in both early and late time point models, we investigated the amount of variation explained by center effects in comparison with other variables separately by time point in logistic models for 3 months, 1 year, and 2 years. In the 3-month model, the generalized R^2 values with and without center effects were 0.07 and 0.05, respectively. The corresponding values at the 1-year time point were 0.13 and 0.03, and for the 2-year time point, they were 0.22 and 0.02. These results demonstrated an increasing effect of individual center practice as the time from donation increased. By 2 years, center effects were 10-fold the effect of all other covariates.

Because A2ALL was an observational study, we postulated that center variation in donor follow-up might be related to differences in the standard of care for the follow-up of non-A2ALL donors. Although all centers and donors agreed to follow the A2ALL protocol, the degree of rigor and resources used to achieve donor follow-up might have varied according to each center's standard of care. Thus, the centers were surveyed to determine their standard of care for long-term donor follow-up, and 7 centers responded. Figure 4 also demonstrates that center practice differed in how long donors were expected to return to the clinic, with 1 center expecting drop-off after the first week and others expecting donors to return as long as 10 years after donation. Although the highest performing center (center F) expected annual follow-up as part of its clinical standard of care through 10 years after donation, even centers whose standard of care did not follow donors beyond 2 years were able to achieve approximately 80% overall follow-up in the A2ALL study. Thus, standard-of-care practices did not fully explain the center variability in A2ALL follow-up success.

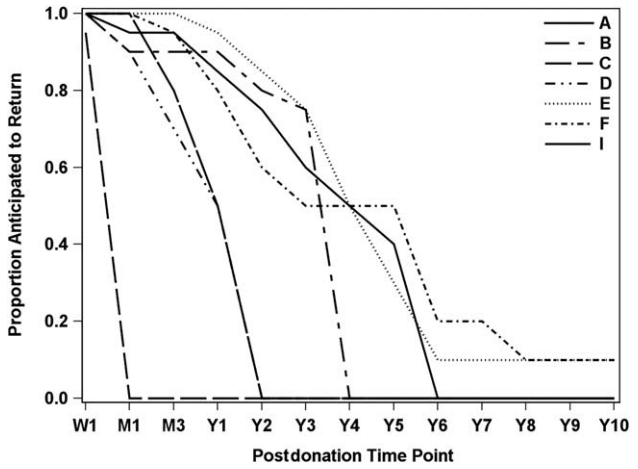

Figure 4. Anticipated follow-up based on usual clinical practice as reported by centers. There were 9 A2ALL centers, but data were not available for 2 centers that were no longer participating in the study at the time of the analysis. The time points after donation were week 1 (W1), month 1 (M1), month 3 (M3), and years 1 to 10 (Y1-Y10).

For the subset of 265 donors who completed at least 1 SF-36 form after donation and had a subsequent expected visit, the PCS and the MCS from the SF-36 were tested as potential predictors of completed follow-up. These donors had a total of 475 forms (average per donor = 1.8, range = 1-4; Table 2). The average PCS and MCS values for this subset of postdonation forms were 54.1 (range = 21-70) and 52.0 (range = −1 to 68), respectively, with higher scores indicating better functioning. Although the ranges were wide, the means were higher than the general population mean of 50 but were within 1 SD (SD = 10). A higher PCS was marginally associated with a lower probability of completed follow-up (OR per 10-unit increase or 1-SD increase in a normative population = 0.74, 95% CI = 0.55-1.00). No significant associations between completed follow-up and MCS were found (OR per 10-unit increase or 1-SD increase in a normative population = 0.99, 95% CI = 0.79-1.23).

DISCUSSION

In summary, living liver donors were very compliant with follow-up for the first year, but follow-up decreased over time in a nonlinear manner. From years 2 to 7, the proportion of completed visits was approximately 70%. There were substantial center differences in completed visits. Although every center agreed to follow the A2ALL protocol, which required annual donor visits to the transplant center, the standard clinical protocol for donor follow-up at each center varied, particularly after the first year. Additionally, centers varied in their use of methods for obtaining information indirectly (ie, telephone and distant visits outside the transplant center).

Patients who missed follow-up did not differ in many ways from those who completed follow-up, and this argues against a substantial systemic bias in the analysis of long-term donor outcomes for those who followed up. However, there were some differences. Donors who missed follow-up in the long-term were more likely to be younger and have a higher PCS on the SF-36. This suggests that donors may be less likely to follow up if they are healthier and do not perceive a need for care. This suggests that data gathered for donors who do follow up will lead to a lower HRQOL than that of the overall target population of all donors, and this is reassuring. Nonwhite race also predicted lower rates of completed follow-up because whites were more than 3 times more likely to follow up during the first year after donation. Although we did not collect socioeconomic data, this may highlight potential economic or cultural barriers to follow-up. The distance from the transplant center could not be calculated because we collected only the state of residence as a variable. When this was analyzed as the same state or a contiguous state versus more than 1 state from the transplant center, it was not predictive of follow-up. However, distances between states vary widely in the different areas between the A2ALL centers; thus, the actual distance may be an unmeasured factor included in the center differences measured. A recipient diagnosis of HCV or HCC also predicted lower rates of follow-up with an OR of 0.34. The reasons for these 3-fold lower odds of donor follow-up are unclear. Although recipient complications and adverse outcomes did not predict follow-up, the recipient diagnosis may be a marker for higher rates of complications due to recurrence in HCV and HCC patients or other unmeasured factors. This phenomenon needs further exploration.

Our data concur with prior data suggesting that quality of life (QOL) is at or above US norms on a general QOL survey[11] and that virtually all are satisfied with their decision to donate, regardless of recipient outcomes.[9,10] Severe psychiatric disturbances have been reported in some living donors from our group, however, and this suggests that ongoing long-term follow-up is needed.[15] Interestingly, centers that achieved $\geq$80% follow-up had donors who were on average younger and had fewer higher grade complications (Tables 1 and 2); these are all factors associated in individual donors with a lower probability of follow-up (Tables 4 and 5). This suggests that some centers are able to overcome the barriers to follow-up and achieve higher rates of long-term follow-up despite covariate mixes that would suggest the opposite. This deserves further investigation.

Our data are limited by the fact that we cannot attribute the reasons for the lack of donor follow-up convincingly. Although centers had agreed to pursue follow-up through the study, there was intercenter and intracenter variability. It is also not possible to derive the reason for the lack of follow-up without contact with those donors (perhaps by an outside party, eg, UNOS) to assess these reasons. Despite these limitations, quantifying the proportion of donor follow-up is important for understanding our limitations in assessing long-term donor outcomes. This was a National Institutes of Health–funded study, so it is likely that our efforts at donor follow-up exceeded what is currently achievable without a change in incentives at the transplant center level or without centralized follow-up by OPTN or the Department of Health and Human Services. However, the ability of some centers to achieve nearly complete donor follow-up (97%) demonstrates that the adoption of best practices can improve donor follow-up and that $\geq$80% can be achieved as suggested in the UNOS guidance document[17] with a combination of motivating donors less likely to follow up (younger, healthier donors) and using the telephone (or other long-distance contact) in addition to clinic visits. Although it is likely that physical follow-up at the transplant center provides more valuable information than phone contact, any contact and particularly QOL data are useful and should be encouraged. It is important to note that there was nearly a 1.5-fold range in physical visits between centers in addition to the nearly 2-fold range in follow-up when phone contact was included. With increased reliability on telemedicine and social networking, this represents a significant opportunity to gain valuable information about long-term donor outcomes and should be included in future research and in OPTN policy. It is important to note that no centers achieved $\geq$80% follow-up with actual physical clinic visits alone after the first year after donation.

In summary, these data suggest that donor follow-up is excellent in the short run and declines over time. A large portion of the variability in donor follow-up is related to center differences and could be improved by protocols for long-distance donor follow-up, including phone contact, cooperation with primary care providers, and perhaps a telemedicine initiative. The fact that donors who missed follow-up visits were more likely to have higher physical QOL and to be younger reassures us that we may not be missing substantial complications. However, longer follow-up and improved center protocols for that follow-up are clearly needed to improve our knowledge of long-term complications after donation and to ensure the long-term health of those donors. Future research should also compare the quality of the data and the value of long-distance initiatives versus physical returns to the transplant sites in order to improve the quality of follow-up and decrease the burden on donors and centers.

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